

HYPERTENSION A CONSIDERATION OF ITS SURGICAL TREATMENT*

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Richard Bright, more than a hundred years ago, after his memorable clinical and pathological studies, reasoned that the production of hypertension was due to an altered quality of the blood; which in turn caused hypertrophy of the heart together with the primary disease in the kidney. Thirty years later Gull expressed the opinion that the underlying cause of hypertension was widespread vascular lesions. Since that time much clinical and experimental evidence has been collected which lends support to both hypotheses. Allbutt and others have advanced clinical conceptions in favour of Gull's view, which, in general, has been accepted in the last twenty-five years by students of the problem of essential hypertension. However, a few investigators—for example, Volhard and Fahr—have expressed the belief that the primary cause of essential hypertension is renal dysfunction. The recent experimental work by Goldblatt lends support to such a hypothesis.

The treatment of hypertension by operation on the sympathetic nervous system has stimulated a new interest in the subject. Fifteen per cent. of all adults are assumed to have hypertension and 23 per cent. of all deaths at an age greater than 50 years are supposed to be directly attributable to this disease. Cardiovascular-renal disease, of which hypertension is an important factor, causes more than four times as many deaths as cancer, and hypertension apparently accounts for more deaths each year than does either cancer or pneumonia. Hypertension is therefore one of the most common and serious conditions that come under the care of physicians, and any therapeutic innovation which may lessen the mortality should be carefully examined. Arterial hypertension is considered to be present when the systolic blood pressure of adults persists at 150 mm. Hg or over. It is probably true that the blood pressure does not increase normally after maturity, and the blood pressure of infants and children is significantly lower than that of adults.

The treatment of hypertension has been complicated by the erroneous opinions that the elevation of blood pressure is not a disease but a symptom, and that the elevation of blood pressure in essential hypertension is beneficial and necessary for normal functioning of organs such as the kidneys. Study of patients whose blood pressure has been reduced to normal by operation at the Mayo Clinic indicates that the kidneys function as efficiently as, or even better than, they did when the pressure was high. In our experience there is no basis for the belief that patients who have essential hypertension feel unwell when the blood pressure is reduced, and we are convinced that it is

extremely desirable to lower the blood pressure in all cases in which it is significantly high.

Secondary Hypertension

Hypertension may be divided into two main groups—secondary, and essential or primary hypertension. Secondary hypertension results from such lesions as pyelonephritis, glomerulitis, hydronephrosis, coarctation of the aorta, and tumours of the suprarenal glands. Primary renal lesions should be excluded by careful study, particularly by intravenous urography, because removal of a diseased kidney may cause the blood pressure to return to normal.

COARCTATION OF THE AORTA

This condition should always be suspected in young persons who have hypertension. This congenital anomaly is characterized usually by normal or low blood pressure in the lower extremities (normally the blood pressure in the lower extremities is significantly higher than it is in the arms), palpable arterial pulsations or bruit in the intra-scapular region, and diminution in strength of pulsations in the arteries of the lower extremities. Roentgenologic examination of the thorax may show absence or deformity of the aortic shadow and erosion of the ribs attributable to development of the large collateral arteries.

TUMOURS OF SUPRARENAL GLAND

Tumours of the suprarenal gland that cause hypertension are comparatively rare. Those of the medulla or medulla-like tissue usually give rise to paroxysms of hypertension, which manifest themselves clinically as episodes of epigastric or substernal pain, pallor, palpitation, tachycardia, and marked elevation of the blood pressure. Since the medullary portion of the suprarenal gland is derived from the embryonic sympathetic nervous system, tumours which involve the medullary portion of the suprarenal gland might be expected to give rise, among other things, to an excessive supply of adrenaline. The most important tumours of the medullary portion of the suprarenal gland are the paragangliomas, which are benign in character, and the syndrome caused by them is characterized clinically by attacks of paroxysmal hypertension.

Five cases of tumour of the medullary portion of the suprarenal gland have been reported in the literature by Donzelot, Robert, Orth, Labbé, Vaquez, Oberling, and Jung. The sixth case, the first in which cure was brought about by operation, was reported by C. H. Mayo (1927). The seventh case, that of Shipley and Pincoffs, was operated on successfully and a large amount of adrenaline was demonstrated in the tumour by biological assay. Cases were subsequently reported by

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Porter, Kalk, and Laubry and Bernal. Bauer, in Vienna, reported a case in which the suprarenal gland was normal, but in the same case Leriche found a paraganglioma the size of a walnut (about 3 cm. in diameter) between the vertebral column and the aorta.

No satisfactory explanation for the paroxysmal character of the hypertension in the cases of paraganglioma has been made. Periodic haemorrhages into the centre of the tumour may force out the adrenaline. Unusual physical exertion such as bending may express adrenaline from the tumour. Emotional reaction such as fear or anxiety, which normally stimulates an increased flow of adrenaline, may in the presence of a paraganglioma provoke an abnormally large discharge of that substance. The complete absence of signs of arteriosclerosis in cases of hypertension caused by paraganglioma is of particular interest as being evidence against the conception that adrenaline plays a part in cases of arteriosclerosis and essential hypertension. Kelly, Piper, Wilder, and Walters (1936) reported a case of suprarenal tumour and paroxysmal hypertension.

Hypertension associated with tumours of the suprarenal cortex is not paroxysmal in type. Obesity, hirsutism, deep voice, and amenorrhoea may be associated changes. Ordinarily the potassium in the blood is low and the sodium is high. Binger and Craig (1938) reported a case of atypical suprarenal tumour.

RENAL LESIONS

One should always suspect the presence of tumours of the suprarenal glands as well as primary renal lesions in cases of hypertension. Barker and Walters (1938) reported a case of hypertension in which the blood pressure became normal after surgical removal of a renal lesion. This was a case of unilateral chronic atrophic pyelonephritis in which hypertension appeared after the chronic pyelonephritis was well developed and the kidney had become atrophic.

The incidental association of chronic pyelonephritis and hypertension is suggested by the experimental work of Goldblatt (1937), who showed that hypertension could be produced by partial obstruction of the flow of blood through the renal artery. The idea that in some cases hypertension may be caused primarily by renal disease, especially if the arterial blood supply of the kidneys has been impaired, has been revived. Complete sympathectomy performed on dogs does not influence the hypertension produced by Goldblatt's technique. An ischaemic kidney of one dog transplanted to the neck of a second dog produced hypertension in the latter. The hypothesis has been advanced that this renal type of hypertension is produced by liberation of some pressor substance from the kidney. Longcope (1937) found definite hypertension in 50 per cent. of twenty-two cases of pyelonephritis. Butler (1937) reported six cases of chronic pyelonephritis associated with hypertension among children. In two cases in which the pyelonephritis was unilateral, nephrectomy was followed by normal blood pressure.

The exact relation of chronic pyelonephritis to hypertension is still debatable. In many cases of chronic pyelonephritis the blood pressures are normal. However, the degree and type of injury to the renal parenchyma may vary greatly in cases of pyelonephritis. It seems reasonable to suppose that in Barker and Walters's case the patient had the capacity for developing hypertension in the first place and that the degree and type of renal damage which would produce it then developed. There was certainly enough evidence of arterial disease in the renal cortex to produce definite obstruction of the renal

circulation. One must consider that the hypothetical pressor substance produced by a kidney rendered ischaemic by Goldblatt's technique might also be produced by some other type of renal injury such as occurs in certain cases of chronic pyelonephritis.

Secondary hypertension, then, is the elevation of the blood pressure that can be attributed to some associated lesion or other condition of the body, whereas essential hypertension is an elevation of the blood pressure in which the cause or aetiological factor is not known.

Essential or Primary Hypertension

In regard to essential hypertension much is known about the mechanism of elevation of the blood pressure. Three factors are responsible for maintaining normal blood pressure, and derangement of any one of these may cause a change in the blood pressure. The cardiac output, the volume or viscosity of the blood, and the resistance offered to the flow of the blood through the peripheral parts of the arterial system determine the blood pressure. It has been proved that cardiac output or viscosity of the blood is not altered in cases of essential hypertension, but that the calibre of the peripheral vessels is decreased. The situation is comparable to a garden hose at the end of which a nozzle is attached. If one decreases the diameter of the opening of the nozzle pressure within the hose increases, as is shown by the greater distance to which the stream is thrown. The decrease in diameter of the peripheral vessels is attributable to (1) a condition inherent in the arterioles, and (2) an abnormal reaction of the arterioles to vasomotor stimuli. Wide fluctuations of blood pressure would be indicative of an abnormal response of arterioles to vasomotor stimuli. A high sustained blood pressure with little fluctuation would be indicative of an inherent or automatic constriction of the arterioles.

There is a large hereditary factor in essential hypertension, as revealed by Ayman (1934), who found that in families in which both parents had absolutely normal blood pressure the incidence of elevated blood pressure among the children was only 3 per cent. In families in which one parent had hypertension the incidence rose to 28 per cent., and in families in which both parents had arterial hypertension the incidence was 45 per cent. Hines has shown that a family history of hypertensive cardiovascular disease is five times more frequent among individuals who have hypertension or who are hyperreactive to a standard stimulus (immersion of the hand in ice-water) than it is among individuals who react normally to the test. The exact inherent quality responsible for this is not known, but probably a hyperreacting sympathetic nervous system responds abnormally and produces unusual vasoconstriction as a result of various emotional stresses and strains.

Hypertension that has been produced experimentally in animals has some characteristics of essential hypertension in man. Goldblatt (1937) has produced hypertension by diminishing the flow of blood to the kidneys of dogs by means of clamps applied to the renal arteries. The hypertension of dogs closely resembles that of man, but complete evidence that it is the exact counterpart is entirely lacking. Those who have accepted the identity of Goldblatt's hypertension in dogs and essential hypertension in man believe that both are due to some chemical or hormonal substance. Up to this time there is no concrete evidence that essential hypertension is due to an abnormal pressor substance, and, reducing the problem of the aetiology of essential hypertension in man to its simplest form

in the light of our very inadequate knowledge of the subject, heredity and the stresses and strains of life seem to be the most important factors.

Essential hypertension has been classified into four groups by Keith and Wagener: (1) slight to moderate increase in the blood pressure, which ordinarily becomes normal as a result of rest, and mild sclerosis of the retinal arteries, usually without symptoms; (2) moderate to severe hypertension, moderate sclerosis of the retinal arteries, and occasionally venous thrombosis; clinical symptoms are present or absent; (3) moderately severe hypertension and angiospastic retinitis, almost always associated with clinical symptoms of hypertension; and (4) severe hypertension, angiospastic retinitis, oedema of the optic disks, and, always, clinical manifestations of hypertension.

This grouping does not indicate the degree of hypertension, although the blood pressure is often higher in one group than in the group which numerically precedes it. The hypertension of any patient may progress from group to group until group 4 is reached. Mortality among patients who have hypertension groups 1 and 2 is 30 to 42 per cent. respectively in four years. Mortality among patients who have hypertension group 3 is 78 per cent. in four years; and in group 4, 98 per cent. (Keith). This high mortality should be noted carefully by those who are inclined to consider that hypertension is not ordinarily a serious disease. Malignant hypertension and essential hypertension are not separate conditions, for malignant hypertension is a type of essential hypertension. The term "malignant" is used loosely to designate severe forms of hypertension.

Medical Treatment of Essential Hypertension

On the whole, medical treatment of hypertension has been unsatisfactory. It has been stated that a great many preparations reduce blood pressure in cases of essential hypertension; however, on close examination it is evident that in most of these instances diminution of the blood pressure supposedly resulting from a specific remedy occurred only as a part of the usual wide fluctuations of blood pressure that are characteristic of essential hypertension. Such drugs as are available for the reduction of blood pressure usually possess unpleasant side effects or short action. The specific need in the medical treatment of hypertension is for a drug which will produce vasodilatation for a comparatively long time (three to six hours) and which does not produce harmful or unpleasant side effects. Sodium nitrite, sodium nitrate, purine derivatives—for example, theobromine and theophylline—iodides, and tissue extracts—for example, padutin (a preparation obtained from the pancreas), liver extract, and adenosin—are of little or no value in the treatment of hypertension. Occasionally when hypertension develops during the menopause it may be reduced by administration of theelin or progynon. However, it is inadvisable to treat such patients with these hormones for long periods unless a definite reduction of the blood pressure rather promptly follows adequate dosage.

Of all the drugs commonly used in the treatment of hypertension the sedatives are the best, and of them phenobarbital is as good as any. The ideal sedative is one that reduces nervousness and irritability but does not interfere with the essential cerebral activities. Ordinarily, $\frac{3}{4}$ grain to $1\frac{1}{2}$ grains (0.05 to 0.1 gramme) of phenobarbital three times a day is advisable.

Comparatively recently a new drug, potassium sulphocyanate, has been introduced for the treatment of essential

hypertension. Its action is uncertain, but it is supposed to produce peripheral vasodilatation. Barker has shown that the blood pressure in about 50 per cent. of hypertensive patients is reduced by careful treatment with potassium sulphocyanate. The amount of this drug that is administered orally should be determined by frequent calculations of the concentration of cyanates in the blood. The concentration in the serum should range between 8 and 12 mg. in each 100 c.cm. of blood. As little as 3 grains (0.2 gramme) or as much as 12 grains (0.8 gramme) of potassium sulphocyanate must be administered each day to cause this concentration in the blood. Barker has described a method for determination of cyanates in the blood; this has been modified by Griffith and Lindauer. Such symptoms as headache, insomnia, and nervousness may be relieved, according to Barker, when the blood pressure is reduced. Fatigue, macrocytic anaemia, and enlargement of the thyroid gland may occur even if administration of the drug is well controlled. If concentration in the blood is too great, lethargy, mental confusion, weakness, difficulty of speech, cutaneous lesions, and collapse may occur.

Experience at the Mayo Clinic with the use of potassium sulphocyanate in the treatment of hypertension has been somewhat limited, but relief of symptoms such as headache is often striking. There is definite reduction of blood pressure in some cases. It is advisable to continue well-controlled treatment for about three months before a decision is made that the treatment is not of value, as blood pressure may decrease slowly in instances in which it is reduced at all. Potassium sulphocyanate should never be administered for a long period unless the amount given is based on studies of concentration of cyanates in the blood. It is imperative for the physician prescribing sulphocyanates to familiarize himself with the literature on the subject before treating the patient with them. Not only does the administration of potassium sulphocyanate help patients who have not had an operation for the condition, but also in some of the cases in which little or no benefit has been obtained from operation its use has been followed by very gratifying results. In some cases in which potassium sulphocyanate was given before operation without benefit the administration of the drug after extensive sympathectomy has produced marked lowering of the blood pressure.

Rest and the reduction of nervous stresses and strains are important in the treatment of many patients who have essential hypertension. In general, it is advisable for such patients to obtain nine hours of rest in bed at night, to lie down for an hour or an hour and a half in the middle of the day, to take vacations frequently, to acquire a calm philosophic outlook on life, and to avoid nervous stresses and strains. Young individuals who follow strenuous occupations may well consider it advisable to change to an occupation that is more restful.

Many diets have been advised in the treatment of hypertension, but there is little evidence that diet influences blood pressure. We do not feel it advisable to restrict protein or salt in diets of hypertensive patients. Individuals who are over weight should reduce, for obesity throws an additional strain on the heart by increasing the work that it must do and as a result of deposition of fat in heart muscle and around the organ. Restriction of intake of alcohol and coffee is not imperative unless they serve as stimulants. They do not themselves increase the blood pressure appreciably. Smoking increases greatly the blood pressure of many patients who have hypertension, and if this can be demonstrated by having the patient

smoke after his blood pressure has reached a basal level it is well to consider sharp restriction or complete elimination of smoking.

Indications for and Results of Surgical Treatment of Essential Hypertension

The surgical treatment of hypertension is based chiefly on the assumption that the increased arteriolar tone can be released by operation on the sympathetic nervous system, thus lowering the blood pressure. Arteriolar tone can be diminished by sympathectomy, as has been established clinically in the treatment of Raynaud's disease and thrombo-angiitis obliterans. Extensive sympathectomy produces two other effects that may be of value in the treatment of essential hypertension (Fig. 1)—namely, an

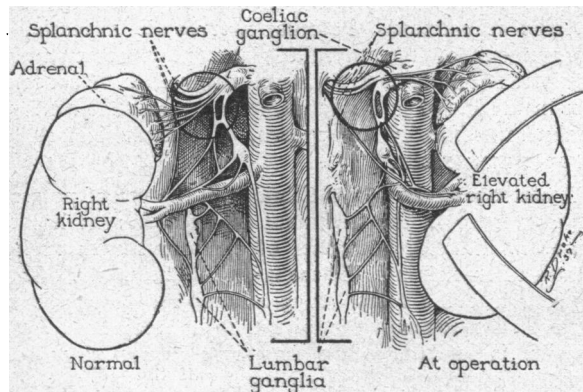


FIG. 1.—Extensive subdiaphragmatic sympathectomy in which the major, minor, and lesser splanchnic nerves with a portion of the coeliac ganglion and upper lumbar sympathetic trunk are removed.

increase in the blood supply to the kidneys and prevention or diminution of spontaneous release of adrenaline from the suprarenal glands. If the type of hypertension experimentally produced in animals by Goldblatt is comparable to essential hypertension in man, extensive sympathectomy is designed to destroy the sympathetic innervation of the kidneys and thus increase the blood supply to them. We believe that sympathetic denervation of the suprarenal glands, which is accomplished as part of the procedure of extensive sympathectomy as performed at the Mayo Clinic (Fig. 2), is probably of value only because it diminishes or prevents episodes of marked release of adrenaline from the suprarenal glands. Whether extensive sympathectomy is more valuable in the treatment of essential hypertension than partial sympathectomy, such as supradiaphragmatic splanchnicectomy (Peet) or coeliectomy (Crile), I do not know, but extensive sympathectomy is a more logical procedure, for it relieves sympathetic control of the kidneys and the suprarenal glands as well as that of the intra-abdominal regions and of a large portion of the lower extremities.

From the discussion stimulated by the papers presented at the last International Surgical Congress in Brussels in a symposium on the surgical treatment of arterial hypertension it was evident that the surgical treatment of hypertension has proved of value in most clinics. Three factors in the causation of essential hypertension were stressed—namely, suprarenal, renal, and vasomotor. Hereditary, constitutional, and psychic factors, as well as the factors linked with certain hyperexcitable conditions of the sympathetic nervous system, were also discussed.

The futility of carrying out extensive sympathectomy in cases of hypertension in which there is irreparable damage to the cardiovascular mechanism is apparent. Nor should operation be considered in a case in which a mild and

slowly progressive disease is amenable to medical treatment. Operation seems most efficacious in the definite vasospastic type of hypertension, in which sharp and brisk elevations in blood pressure occur when the hands are immersed in cold water, and in cases in which a marked fall in blood pressure is produced when pentothal sodium, sodium amytal, or a nitrite is administered. As an average rule the patient must be less than 50 years of age and the hypertension must be classed as of group 2 or 3.

One group of patients whose records seem discouraging are symptomatically relieved, especially of headaches. In one such case the pre-operative studies indicated little decrease in blood pressure and the post-operative blood-pressure readings were disappointing, but the patient was

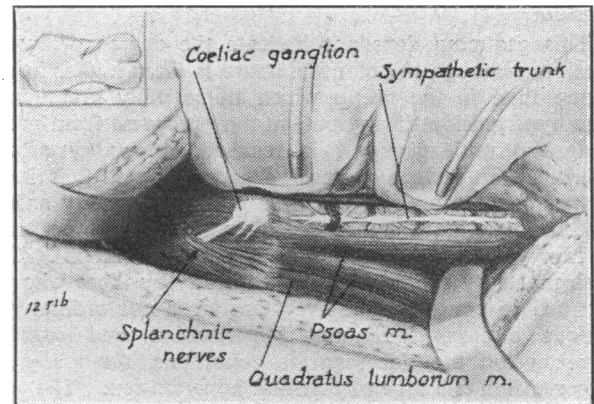


FIG. 2.—Resection of a portion of the twelfth rib and exposure of splanchnic nerves, coeliac ganglion, and lumbar sympathetic trunk; inset, incision employed.

completely free from a disabling headache for eighteen months following operation.

The contraindications to extensive sympathectomy are congestive heart failure, angina pectoris, marked renal insufficiency, and advanced arteriosclerosis. The operative mortality is negligible in properly selected cases, and, although some of the patients eventually die of the disease, operation seems neither to have hastened nor to have delayed death. Experience with 237 patients who have undergone extensive sympathectomy without an operative death has demonstrated that the operation, as performed at the Mayo Clinic after careful examination and selection, has a definite place in the treatment of essential hypertension. The symptomatic relief following operation has exceeded the effect on blood pressure. The proportion of patients relieved of headache when the effects of the operation on the blood pressure are recorded as good, fair, or poor was as follows: 100, 80, and 76 per cent. respectively. Nervousness was relieved after operation when the effect of operation on the blood pressure was recorded as good, fair, or poor, in 80, 66, and 67 per cent. of cases respectively. The proportion of patients relieved of non-anginal pain in the left side of the thorax after operation when the effects of operation on the blood pressure were recorded as good, fair, or poor was 90, 75, and 60 per cent. respectively. Fatigue on exertion was relieved after operation in 41, 44, and 50 per cent. when the effect of operation on the blood pressure was recorded as good, fair, or poor respectively; while dyspnoea on exertion was relieved in 50, 46, and 48 per cent. These figures bear out in a striking manner isolated clinical observations that frequently patients are relieved of such distressing symptoms as headache, in spite of the fact that reduction of their blood pressure does not seem apparent. The results of the operation for hypertension in the 237

cases were classed as follows: failure in 20 per cent., temporary relief in 28 per cent., fair results in 28 per cent., and good results in 24 per cent.

The women obtained good or fair results from operation in a slightly higher proportion of cases than the men, the percentages being 55 and 48 respectively. The duration of the hypertension before operation did not influence significantly the effect of operation. In contrast to previous conceptions regarding the influence of age, this factor did not seem to influence the good or fair results, although patients in the third decade of life received a slightly smaller percentage of good or fair results than did those in the fourth, fifth, and sixth decades.

Allen, Lundy, and Adson (1936) reported a case in which operation was followed by lowered blood pressure until pregnancy occurred. After interruption of the pregnancy the blood pressure decreased to the previous level. The inference to be drawn from this case is that hypertension can be caused from toxæmias and can act, with regard to sympathectomy, in a manner similar to Goldblatt's experimental animals. There seems, therefore, to be some difference in the mechanism of production of essential hypertension and of the hypertension that occurs as a part of toxæmia of pregnancy. Allen, Lundy, and Adson concluded that until more was known about the subject it was probably desirable for patients operated on for hypertension to avoid pregnancy if possible; if such patients become pregnant careful observation of the blood pressure should be made, and if there is any evidence of an increase the pregnancy should be terminated.

Since this case was reported several women who have had extensive sympathectomy for hypertension have completed their pregnancies successfully without any change in blood pressure, and therefore we have come to the conclusion that if a patient who has had a sympathectomy for hypertension becomes pregnant the pregnancy should be allowed to continue until toxæmia and increasing blood pressure indicate an impending danger.

In analysing the results of surgical treatment by extensive sympathectomy it is evident that fixed rules with regard to the selection of cases for operation are difficult to formulate. In general it can be said that patients probably will obtain good results from operation when the diastolic blood pressure decreases pre-operatively to less than 110 mm. Hg as a result of rest, administration of sodium amylal, and injection of pentothal sodium, and when sclerosis of the retinal arteries is absent or slight. Also, the probabilities that a patient will secure good results from operation are small in the presence of advanced sclerosis of the retinal arteries, when the maximal diastolic blood pressure exceeds 150 mm. Hg, or when the diastolic pressure does not decrease to less than 120 mm. as a result of rest, intravenous injection of pentothal sodium, or administration of sodium amylal. It has been demonstrated that operation can be carried out safely. The operation does not disable, and it often produces remarkable effects on blood pressure.

Comment and Summary

In the treatment of hypertension, primary or essential hypertension, which exists in 85 per cent. of cases, and secondary hypertension, which is present in 15 per cent. of cases, must be considered. Secondary hypertension results from such lesions as pyelonephritis, glomerulitis, hydronephrosis, coarctation of the aorta, and tumour of the suprarenal glands. The surgical treatment of essential hypertension is based on the assumption that increased

arteriolar tone can be reduced by operation on the sympathetic nervous system, and thus lowering of the blood pressure is effected. Two other effects of surgical treatment that may be of value in the treatment of essential hypertension consist of an increase in the blood supply to the kidneys and prevention or diminution of the flow of adrenaline from the suprarenal glands. In analysing the surgical results it has been found that patients who suffer from a high fixed blood pressure associated with cardiac and renal damage do not obtain enough improvement from operation to warrant its use. Patients whose blood pressure tends to decrease with rest and after administration of sedatives on pre-operative observation have proved suitable for serious consideration of operative treatment. A decrease of both the systolic and diastolic blood pressures is important, and the best results have been obtained when the diastolic pressure decreases to less than 110 mm. Hg under observation. Results have been classified as good, fair, and poor. Included in the good results are those patients whose blood pressure has returned to normal or nearly to normal and has remained so for long periods of time. In addition, relief of symptoms was also noted. Fair results are considered to have been obtained in cases where there is a small reduction of blood pressure with relief of symptoms over long periods of time. Those patients who have experienced a slight or moderate decrease of blood pressure with temporary relief of symptoms are adjudged to have obtained poor results.

In considering the results of surgical treatment of essential hypertension, it is apparent that the operation is of a physiological rather than a pathological nature and that the post-operative response depends on the amount of associated pathological changes in the peripheral vessels, heart, and kidneys.

In analysing the surgical results it is also necessary to keep in mind that patients who suffer from progressive hypertension face a four-year mortality rate of 30 per cent. in group 1, 42 per cent. in group 2, 78 per cent. in group 3, and 98 per cent. in group 4. Although sympathectomy may not be the ideal remedy, there is much evidence that it may prevent or delay complications that all too frequently cause death in the most productive period of the patient's life.

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